IN THE CLAIMS

Please amend the claims as follows:

- (Currently Amended) A method for detecting [[for]] the presence of antibiotic resistant Staphylococcus bacteria from total unamplified Staphylococcus genomic DNA in a sample, the sample comprising a wild type mecA gene sequence or fragment thereof, one or more mutant mecA gene sequence or fragment thereof which differ from the wild type mecA gene sequence by at least one nucleotide, or both, the method comprising the steps-of:
- a) providing an addressable substrate having bound thereto (i) wild-type capture oligonucleotides having a sequence that is complementary to at least part of a first portion of [[the]] a wild-type mecA gene sequence or fragment thereof, and (ii) one or more mutant capture oligonucleotides having a sequence that is complementary to at least part of a first portion of [[the]] a mutant mecA gene sequence which differs from the wild-type mecA gene sequence by at least one nucleotide or fragment thereof, wherein the first portion of the wild-type mecA gene sequence corresponds to the first portion of the mutant mecA gene sequence;
- providing a detection probe comprising detector oligonucleotides bound to a gold nanoparticle, wherein the detector oligonucleotides have a sequence that is complementary to at least part of a second portion of the mecA gene sequence or fragment thereof of [[step]] (a);
- c) contacting [[the]] a sample <u>suspected of having unamplified genomic DNA from an antibiotic resistant Staphylococcus</u> bacteria with the substrate and the detection probe under conditions that are effective for (i) the hybridization of the capture oligonucleotides to the first portion of the mecA gene sequence or fragment thereof, (ii) the hybridization of the detection probe to the second portion of the mecA gene sequence or fragment thereof, and (iii) the discrimination between the wild-type mecA gene sequence or fragment thereof and said one or more mutant mecA gene sequence or fragment thereof that differ by at least one nucleotide; and
- d) detecting whether the gold nanoparticle is associated with an address on the substrate having the one or more mutant capture oligonucleotides that are contacted with the sample, wherein detection of the gold nanoparticle at an address on the substrate having the one or more mutant capture oligonucleotides contacted with the sample is indicative that the sample

Filing Date: December 12, 2003 Title: DIRECT SNP DETECTION WITH UNAMPLIFIED DNA

has genomic DNA from an antibiotic resistant Staphylococcus bacteria eapture oligonucleotide and detection probe hybridized with the first portion and second portions of the meeA gene sequence or fragment thereof.

- (Currently Amended) The method of claim 1, wherein the <u>mutant</u> mecA gene sequence or <u>fragment thereof</u> comprises a Single Nucleotide Polymorphism <u>relative to the wild-</u> type mecA gene sequence.
- (Currently Amended) The method of claim 1, wherein the <u>capture</u> <u>oligonucleotide comprises the</u> single nucleotide difference is recognized by the capture oligonucleotide bound to the substrate.
- (Currently Amended) The method of claim I, wherein the <u>detector</u> <u>oligonucleotides comprise the</u> single nucleotide difference is recognized by the detector oligonucleotides.
 - (Cancelled).
- (Currently Amended) The method of claim 1, wherein the substrate comprises a
 plurality of capture oligonucleotides-each of which can recognize a comprising different single
 nucleotide polymorphisms polymorphism.
- (Currently Amended) The method of claim 1, wherein the sample comprises
 more than one mecA gene sequence or fragment thereof, each of which comprises one or more
 different single nucleotide polymorphisms.
- (Currently Amended) The method of claim 1, wherein one or more types of detector probes are provided, each of which has detector oligonucleotides bound thereto that are capable of hybridizing to the mecA gene sequence or fragment thereof.
- 9. (Withdrawn) The method of claim 1, wherein sample is contacted with the detector probe so that a nucleic acid target present in the sample hybridizes with the detector oligonucleotides on the detector probe, and the nucleic acid target bound to the detector probe is

Title: DIRECT SNP DETECTION WITH UNAMPLIFIED DNA

then contacted with the substrate so that the nucleic acid target hybridizes with the capture oligonucleotide on the substrate.

- 10. (Currently Amended) The method of claim 1, wherein sample is contacted with the substrate so that the mecA gene sequence or fragment thereof present in the sample hybridizes with the capture oligonucleotide, and the mecA gene sequence or fragment thereof bound to the capture oligonucleotide is then contacted with the detector probe so that the mecA gene sequence or fragment thereof hybridizes with the detector oligonucleotides on the detector probe.
- (Withdrawn) The method of claim 1, wherein the sample is contacted simultaneously with the detector probe and the substrate.
 - (Cancelled).
- (Currently Amended) The method of claim 1, wherein the detection is probe allows detection by photonic, electronic, acoustic, opto-acoustic, gravity, electrochemical, electro-optic, mass-spectrometric, enzymatic, chemical, biochemical, or physical means.
 - 14.-26. (Cancelled).
- (Previously Presented) The method of claim 1, wherein the detecting comprises contacting the substrate with silver stain.
- (Previously Presented) The method of claim 1, wherein the detecting comprises detecting light scattered by the nanoparticle.
- (Previously Presented) The method of claim 1, wherein the detecting comprises observation with an optical scanner.
- 30. (Previously Presented) The method of claim 1, wherein the detecting comprises observation with a flatbed scanner.

- 31. (Original) The method of claim 29 or 30, wherein the scanner is linked to a computer loaded with software capable of calculating grayscale measurements, and the grayscale measurements are calculated to provide a quantitative measure of the amount of nucleic acid detected.
- 32. (Previously Presented) The method of claim 1, wherein the oligonucleotides attached to the substrate are located between two electrodes, the nanoparticles are made of a material that is a conductor of electricity, and step (d) comprises detecting a change in conductivity.
- (Original) The method of claim 32, wherein the electrodes are made of gold and the nanoparticles are made of gold.
- (Original) The method of claim 32, wherein the substrate is contacted with silver stain to produce the change in conductivity.
- 35. (Currently Amended) The method of claim 1, wherein a plurality of capture oligonucleotides, each of which can recognize a different mecA gene sequence or fragment thereof are attached to the substrate in an array of spots and each spot of oligonucleotides is located between two electrodes, the nanoparticles are made of a material that is a conductor of electricity, and step (d) comprises detecting a change in conductivity.
- (Original) The method of claim 35, wherein the electrodes are made of gold and the nanoparticles are made of gold.
- (Original) The method of claim 35, wherein the substrate is contacted with silver stain to produce the change in conductivity.
 - 38,-167. (Cancelled).
- 168. (Previously Presented) The method of claim 1, wherein the substrate further comprises one or more capture oligonucleotides having sequences that are complementary to Tuf gene, 16S rRNA gene, or both, or to fragments thereof.

distinguish between two or more species of a common genus.

169. (Previously Presented) The method of claim 168, wherein the method is used to

- 170. (Previously Presented) The method of claim 169, wherein the species differ by two or more nonconsecutive nucleotides.
- 171. (Previously Presented) The method of claim 169, wherein the species differ by two or more consecutive nucleotides.
- 172. (Previously Presented) The method of claim 169, wherein the species differ by at least one nucleotide.
- 173. (New) The method of claim 1 wherein the sample does not comprise amplified mecA DNA.
- 174. (New) The method of claim 1 wherein the amount of the sample and the conditions are effective to detect unamplified genomic mecA DNA.